REMARKS

1. Status of the Claims

Claims 1, 4-13, and 16-19 are currently pending. Pursuant to the Examiner's request, Applicant has amended the claims to properly reflect that claims 2-3 and 14-15 were previously cancelled. Claims 5, 11 and 17-19 have been amended to remove the reference to increased oil content in the transgenic plants. New claims 20-26 have been added. Support for the newly added claims may be found at pages 4, 7 and 12 of the Specification and Figure 3. No new matter has been added.

2. Specification

The Examiner has indicated that the Specification is objectionable because the Applicant has attempted to improperly incorporate subject matter into the text of the Specification by referring to GenBank Accession numbers. Referring to MPEP 2422.03 and 37 C.F.R. §1.821(d), the Examiner argues that any sequences discussed within the application must be included in the Sequence Listing. Applicant disagrees. The Sequence Listing rules referred to by the Examiner do not require an Applicant to include these sequences in a Sequence Listing. Prior art sequences referred to in a given application by name and a publication or accession reference need not be included as part of the Sequence Listing. MPEP 2422.03, paragraph 5. There is nothing improper in describing sequences that have been previously disclosed by referring to publications or their deposit or accession numbers. Reconsideration and removal of the objection is, therefore, respectfully requested.

3. Claim Rejections under 35 U.S.C. § 112, first paragraph

A. Written Description

The Examiner has again rejected existing claims 1, 4-13 and 16-19 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner

argues that the Applicant has only disclosed or described the cDNAs of three ADP/ATP translocators (two from *Arabidopsis* and one from *S. Tuberosum*) but the claims are broadly directed to genetically modified plant cells comprising any foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator integrated into the nuclear genome, transformed plants thereof and methods of producing increased starch and oil in transformed plants therewith. The Examiner has argued that the Specification does not provide adequate written support for the use of any foreign nucleic acid molecule because the Applicant has failed to describe a representative number of foreign nucleic acid molecules encoding a plastidial ADP/ATP translocator falling within the scope of the claimed genus. Applicants respectfully traverse.

The Examiner relies heavily on the recent Federal Circuit decisions interpreting the application of the written description requirement to inventions in the field of biotechnology. Citing to *University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1938, 1406 (Fed. Cir. 1997), the Examiner asserts that the Applicant is not entitled to a genus of cDNAs encoding plastidial ADP/ATP translocators because they have failed to describe a representative number of species or to describe the specific structural features common to the members of the genus.

First, it is important to note each case involving the issue of written description must be decided on its own facts and that the precedential value of cases in the area of written description is extremely limited. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555 (Fed. Cir. 1991). Secondly, it is important to recognize that this inquiry is conducted from the perspective of the skilled artisan. Possession is a fact-based inquiry and necessarily depends on the nature of the invention claimed. Unlike the claims in Eli Lilly which were specifically directed to the isolated cDNAs, the present claims are directed to genetically modified plant cells or plants comprising any foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator integrated into the nuclear genome and methods of producing plants with increased starch and amylose content. Contrary to the Examiner's opinion, Applicant submits that the skilled artisan would recognize that the inventors had provided sufficient written description to evidence possession of the claimed genus in view of the Applicant's disclosure and his general knowledge of the art.

As noted in Applicant's prior response, the Specification clearly states that any nucleic acid molecule encoding an ADP/ATP translocator, which, after expression, is localized in the inner membrane of plastids, can be used to transform plant cells to achieve the results of the present invention. A person of ordinary skill in the art, after reading the disclosure, would understand that the Applicant clearly recognized and taught that any foreign nucleic acid molecule encoding an ADP/ATP translocator, which is localized to the plastid, would achieve the desired purpose. The Examiner argues that the Applicant is not entitled to claims of this scope because they have failed to describe or define the structural features and elements necessary for plastidial ADP/ATP translocator activity. In other words, Applicant has failed to describe defining motifs, conserved regions, etc. shared by members of the claimed genus. Applicant disagrees. Applicant submits that the disclosure and Figures 3 and 4 provide exactly this type of information. Moreover, Applicant submits that the contemporaneous and prior art publications sufficiently characterized and described nucleic acid molecules from various species which encode the ADP/ATP translocator proteins encompassed by claims. These types of proteins and their specific activities have been well documented in the art. Thus, a person of ordinary skill in the art would already be aware of these common or shared characteristics amongst members of the genus and Applicant is not required to reproduce the same in his application.

Adenylate transporters have been well described in the art and are divided into three general categories: the mitochondrial ADP/ATP carrier (AAC) which in their functional state form a homodimer from the monomer that has six transmembrane domains; the plastidial ADP/ATP transporters which reside in the inner envelope membrane of plant plastids and bacterial non-mitochondrial adenylate transporters (e.g. the rickettsial and chlamydial ADP/ATP transporters). The second and third categories of adenylate transsporters share a high structural similarity in that they both belong to the 12 transmembrane domain family of solute transporters. There are numerous prior art publications describing the 15 known members, plant and bacterial, of this transporter family. (*See*, Trentmann et al., Eur. J. Biochem., 267(13), p. 4098 (2000) for a discussion of the state of the art. *See, espectally*, the bibliography of references). Many of these

plant and bacterial ADP/ATP translocator proteins are also referred to in the present application. (See, pages 4-6).

The Specification sets forth the common functional feature or characteristic that must be shared by the genus of foreign nucleic acid molecules. As seen on page 6, the foreign nucleic acid molecules must encode a "plastidial ADP/ATP translocator is a transport protein which is localized in the inner membrane of plastids ... and which catalyzes the transport of ATP into plastids and of ADP out of the plastids (see also page 7, line 12). The Specification also refers to several examples of known foreign nucleic acid molecules that encode translocator proteins possessing the desired activity. (See, page 4). Applicant further submits that the Specification also discusses the shared features amongst members of the genus. For example, the Specification teaches that the cDNA encoding an ADP/ATP translocator from Arabidopsis (i.e. AATP1) and the ADP/ATP translocator from *Rickettsia prowazekii* share a 66% similarity. Figures 3 and 4 provide more information about the defining motifs, conserved regions, etc. shared by the proteins encoded by the cDNAs from Arabidopsis thaliana (AATP1 and AATP2) and *Rickettsia prowazekii* ($TCLR_p$). A review of the sequence comparison data in Figure 3 and the hydropathy data in Figure 4 reveals that the proteins share several highly conserved regions and sequence motifs. This is further discussed in the contemporaneous publication to Mohlmann et al. (Eur. J. Biochem 252, 353-359 (1998).

The skilled artisan would, therefore, be aware of the following facts from the data in the Specification and the prior art: (1) the amino acid sequences of the translocator proteins exhibit varying degrees of similarity but there are a number of highly conserved amino acid sequence motifs in the structural part of both plastidic and bacterial ADP/ATP translocator proteins; (2) the peptides AELWG (fourth transmembrane domain of $TCLR_p$), FANQIT (between the fourth and fifth transmembrane domains of $TCLR_p$), NLVE (seventh transmembrane domain of $TCLR_p$) and GKSGGA (eleventh transmembrane domain of $TCLR_p$) are present in all transporters; and (3) the amino acid sequence of AATPI between amino acid positions 155 and 308 is nearly identical to corresponding sequences in AATP2. Mohlmann et al. specifically recognize that these conserved sequences amongst rickettsial and plant transporters are of high importance for the function of the ADP/ATP transporter.

An applicant is not required to describe in detail that which is not new or not conventional. MPEP 2163 citing *Hybridtech v. Monoclonal* Antibodies, 802 F.2d at 1384, 231 USPQ at 94. The MPEP citing *Vas-Cath* further states that the written description requirement is met "if a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the Specification . . .". Applicant submits that, in the instant case, the skilled artisan would, indeed, recognize that any foreign nucleic acid encoding a plastidial ADP/ATP transporter protein would be useful for purposes of the invention in view of the general knowledge within the art regarding the structural features common to plant and bacterial adenylate transporters and the further description in the Specification discussed above. In view of the foregoing remarks, Applicant submits that the Specification provides full written description support for the genus of the claims and respectfully requests reconsideration and removal of the rejection.

B. Enablement

The Examiner has also rejected claims 1, 4-13 and 16-19 under 35 U.S.C. §112, first paragraph, because the Specification while being enabling for transgenic potato plants comprising the AATP1-cDNA from Arabidopsis showing increased levels of starch and percent amylose does not reasonably provide enablement for any plant cells or plants comprising any foreign nucleic acid molecule encoding any plastidial ADP/ATP translocator having any combination of increased levels of oil, starch and amylose or any methods of increasing yield in a transgenic plant or for the production of increased oil in a transformed plant. Simply stated, the Examiner asserts that the claims are not enabled and that undue experimentation would be required to make and use the invention. Applicant respectfully disagrees.

After reviewing the Examiner's comments on pages 6-11 of the Office Action, it appears that the Examiner's enablement rejection can be divided into two parts or issues. The first issue is whether the Applicant has fully described and enabled genetically modified plant cells comprising a foreign nucleic acid molecule encoding a plastidial ADP/ATP translocator

integrated into the nuclear genome wherein the transformed plant or plant cell has an increased oil content in comparison to a non-transformed plant. Applicant submits that this first issue is now moot in view of Applicant's amendments to the claims. The claims are no longer directed to transformed plants or plants cells exhibiting an increased oil content.

The second issue is whether the Applicant has adequately described how to identify other foreign nucleic acid molecules encoding plastidial ADP/ATP translocators which would be suitable for use in the invention and whether these cDNAs encoding plastidial ADP/ATP translocators would be capable of producing plants, other than potato, with increased levels of starch or altered amylose content. As acknowledged by the Examiner, the examples in the Specification describe a method for producing potato plants using the AATP 1 cDNA from *Arabidopsis*. Potato was used and described in the Specification because it is a model species which is relatively easy to transform and because it possesses a large heterotrophic storage organ (the tubers). But, this does not mean that the invention is confined solely to creating trangenic potato plants. The Specification clearly states that the invention would be equally applicable to other plant species (e.g. cells from starch-synthesizing or starch-storing plants such as cereals (rye, barley, oat, wheat, millet, sago, etc.), rice, peas, maize, medullar pea, cassava,. potato, rape, soy bean, hemp, flax, sunflower or vegetables) (see page 8 of the Specification).

A person of ordinary skill in the art would recognize that plant starch biosynthesis takes place exclusively in the plastids that are the sole location of starch synthases and starch-branching enzyme. The skilled artisan would be equally aware of the different metabolic pathways leading to starch accumulation. (*See, e.g.,* Tjaden, J., The Plant Journal (1988) 16(5), 531-540). The level of knowledge in the art coupled with the teachings and examples of the instant Specification would lead a person of ordinary skill in the art to reasonably conclude or expect that the application of the method in these other plant species would result in an increase in starch or amylose content and, thus an increased yield. On page 10 of the Office Action, the Examiner appears to argue that the Applicant has not fully demonstrated that the transformed plants exhibiting an increased ADP/ATP translocator activity will have an increased yield especially since they have not demonstrated that the overexpression of the foreign nucleic acid molecules encoding a plastidial ADP/ATP translocator will result in an increased oil content.

Applicants would simply point out that the claims are no longer directed to increased oil content and that the term "increased yield", in the present context, is defined on pages 9-10 of the Specification, to relate to an increase in the starch content and/or an increase in the amylose content as compared to a wild-type plant.

Applicant submits that the Specification satisfies the enablement requirement as it describes various methods well known to persons of ordinary skill in the art which would allow for the identification and isolation of other foreign nucleic acid molecules encoding a plastidial ADP/ATP translocator protein for use in the claimed method. The Examiner has argued that there is great unpredictability in isolating these nucleic acid molecules (see page 8 of the Office Action) and that undue experimentation would be required. Again, Applicant disagrees. From the description on pages 7-8 of the Specification, the skilled artisan would recognize that the identification of other plastidic ADP/ATP translocators (i.e. non-potato) can be accomplished by screening the cDNA library of other plant species with a gene-specific probe and sequencing the cDNA. Applicant has not asserted that the identification of a cDNA with a high degree of identity to a plastidic ADP/ATP transporter, in and of itself, means that a functional homologue has been identified. As discussed in the Specification, to identifiy a suitable foreign nucleic acid molecule, the skilled artisan would have (1) to express the nucleotide sequence in *E. coli* or yeast and (2) check the activity of the expressed product in proteoliposome reconstitution experiments before concluding that the putative translocator satisfied the functional requirement of the claims. (see page 7, lines 7-10 of the Specification). Contrary to the Examiner's arguments, the procedure for identifying other putative translocators is not the "mere germ of an idea" and Applicant has not attempted to rely solely upon the knowledge of one skilled in the art. As discussed above, the disclosure itself adequately teaches one of ordinary skill in the art how to make and use the claimed invention. The fact that the skilled artisan must screen numerous candidates or conduct complex experiments does not mean that undue experimentation is required especially in fields, such as biotechnology, where such experimentation is routine. MPEP 2164.01. Furthermore, the fact that the Applicant has not described the techniques involved in the making and screening of cDNA libraries and testing for ADP/ATP translocator activity or locating sequences having putative translocator activity in pubic databases using methods of structure function predictions is not fatal in an enablement analysis. It is axiomatic that the test for enablement is "whether one reasonably skilled in the art could make or

use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." It is also well settled that a patent, need not teach, and preferably omits, what is well known in the art. Applicants submit, and the Examiner must agree, that there is a high level of skill within the art. The Examiner must also acknowledge that each of these techniques was well-known and apparent to the skilled artisan and, as such, need out be set forth in intricate detail in the Specification. In view of these facts, Applicant submits that the skilled artisan could readily prepare and screen cDNA libraries using a probe from e.g. AATP1 to identify candidate foreign nucleic acid molecules encoding putative ADP/ATP translocators and then conduct expression experiments to confirm that they possess the required functionality without engaging in undue experimentation. As such, Applicant submits that the full scope of the claims are enabled by the Specification and respectfully request reconsideration and removal of the rejection.

Favorable consideration and early allowance of all the claims is respectfully requested.

Should there by any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,300) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee of $950.00 to be charged to Deposit Account No. 02-2448.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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